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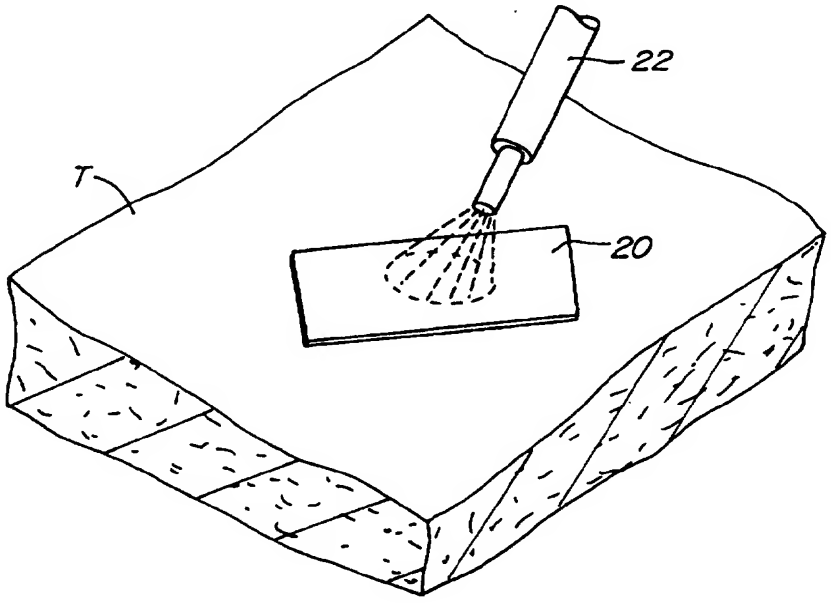

(57) Abstract

A matrix material (12) containing a non-biologic polymer component is fused to tissue (T) by first placing the matrix material (12) over a target location (W) on the tissue and then applying energy to the matrix material. The non-biologic polymer component is of a type where the energy is applied in an amount which together result in fusion of the matrix to the tissue.

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METHODS AND ARTICLES FOR FUSING MATRIX LAYERS CONTAINING NON-BIOLOGIC POLYMERS TO TISSUE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates generally to methods and articles for fusing matrix materials to form layers over tissue. More particularly, the present invention relates to fusing matrix layers containing non-biologic polymers to tissues for wound closure, and other purposes.

The application and fusing of material layers to tissue is useful for a number of purposes. Of particular interest to the present invention, matrix materials may be applied to tissue in order to effect or enhance wound closure, to augment and repair tissue defects, and the like. A variety of specific compositions and methods have been devised for such purposes. For example, the fusing of collagen and other proteins by the application of laser and other energy sources has been suggested for the closure of wounds. See, for example, U.S. Patent Nos. 5,156,613; 5,209,776; and 5,071,417. The application of pre-polymer materials followed by light-induced cross-linking has also been proposed. See, for example, PCT publications WO 94/24962 and WO 94/21324.

While holding great promise, such methods and compositions for the placement of matrix materials on tissue could be improved in a number of respects. For example, it would be desirable to provide improved materials which fuse or adhere to the underlying tissue with an enhanced bonding strength upon the application of energy. It would also be desirable to provide materials having enhanced tensile strength, both before and after the application of energy. Such materials should also possess a degree of elasticity and conformability to enhance positioning and adherence to the underlying tissue, particularly when the tissue undergoes movement which can stress the matrix material. The materials should further be biocompatible and, at least in some

instances, biodegradable so that they can be resorbed or degraded over time.

The subject matter of the present application is related to that of the following commonly owned copending applications: USSN 08/303,336 (published as WO 96/07355 on March 14, 1996); USSN 08/481,712 (published as WO 96/07356 on March 14, 1996); USSN 08/673,710, filed on June 19, 1996; USSN 60/011,898, filed on February 20, 1996; USSN 08/704,852 (Attorney Docket No. 17067-002000), filed on August 27, 1996; and USSN 60/_____ (Attorney Docket No. 17067-002100), filed on October 21, 1996. The full disclosures of each of these applications are incorporated herein by reference.

It would thus be desirable to provide methods and articles for fusing matrix layers to tissue which are improved in at least one or more of the aspects listed above.

SUMMARY OF THE INVENTION

The present invention provides improved methods and articles for fusing a matrix material to tissue for a variety of purposes, including wound closure, tissue augmentation, or the like. The matrix material comprises a non-biologic polymer component which when placed over a target location on the tissue will fuse to the tissue upon the application of energy, such as radio frequency energy, laser energy, ultrasonic energy, heat, infrared, microwave or the like. The energy will be applied in an amount sufficient to fuse the matrix material to the underlying tissue with a peel bond strength of at least about 0.03 N/cm. Thus, as used herein, the terms "fuse" and "fusing" will mean that the matrix material has been caused to adhere to the underlying tissue with a peel bond strength (defined below) of at least about 0.03N/cm. Although the precise energy level will depend on the nature of the non-biologic polymer, the nature of the energy source and the nature of the underlying tissue, typically it will be in the range from about 1 W/cm^2 to about 100 W/cm^2. As used herein, the phrase "non-biologic polymer" will be defined to include polymers produced *in vitro* by chemical reaction between two or more monomers, usually in the

presence of heat and a catalyst. The non-biologic polymers will usually be in the form of polymer synthetic resins having molecular weights above 10 kD, usually in the range from 25 kD to 500 kD. Exemplary non-biologic polymers include acrylates and acrylic resins, such as polyacrylic acid, polyhydroxyethyl-methacrylates, and polyacrylamide; polyvinyl resins, such as polyvinyl alcohol (PVA) and polyvinylpyrrolidone; poly-organic acids and lactanes such as polylactate-glycolides and polycaprolactones, polyethylene oxides; and polypropylene oxides.

The matrix material may be applied (prior to exposure to energy) in a variety of forms, including a solid, mesh, or composite layer. Alternatively, the matrix material may comprise a dispersible, non-solid phase, such as liquids, gels, sols, suspensions, powders, and the like. Preferably, the exemplary non-biologic materials will be in the form of hydrogels are capable of forming (in combination with aqueous media) when applied to the tissue or skin prior to the application of energy. In some cases, the matrix material may comprise substantially pure non-biologic polymer(s), but in many cases it will be desirable to combine additional components, such as carrier materials, reinforcement materials, plasticizers, and the like. After the application of energy, a layer of the matrix material will usually fuse to the underlying tissue with the requisite peel bond strength. The layer will typically have a thickness of at least about 0.01 mm, usually being in the range from about 0.05 mm to about 0.1 mm, and the layer will usually form a substantially continuous surface on the underlying tissue. The area may vary widely, typically being at least about 0.05 cm^2, usually being in the range from about 1 cm^2 to about 100 cm^2.

Articles according to the present invention comprise a sheet of the matrix material generally as described above. The sheets will usually be sterilized and present in a sterile package for distribution and storage prior to use.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a perspective view of a sheet of matrix material according to the present invention.

Fig. 2 is a top view of a package containing the matrix material of Fig. 1, shown with a portion broken away.

Fig. 3 is a schematic illustration of a region of tissue having a wound therein.

Fig. 4 illustrates the method of the present invention wherein a solid sheet of matrix material is placed over the wound of Fig. 3 and radio frequency (RF) energy is used to fuse the matrix material to the tissue.

Fig. 5 illustrates an alternative embodiment of the method of the present invention, wherein a liquid or gel matrix material is applied using a syringe to the wound in the tissue of Fig. 3.

Fig. 6 illustrates the application of RF energy to the liquid matrix material of Fig. 5.

Fig. 7 illustrates a resulting layer of matrix material which has been bonded to tissue according to the method of the present invention.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

Methods and articles according to the present invention may be used for fusing matrix materials to tissue for a variety of purposes. Tissues include virtually all human and animal body tissues, including the skin (epidermis), as well as the external and internal surfaces of virtually all body organs. The present invention is particularly useful for fusing matrix materials to fragile body organs, such as lungs, stomach, liver, spleen, intestines, colon, fallopian tubes, esophagus, ovary, uterus, bladder, and the like. The matrix material may be applied for a variety of purposes, including wound closure, tissue augmentation, and the like. Wounds to be treated may result from accidental trauma, surgical intervention, or virtually any other cause. Tissue augmentation will usually be performed to fill or cover regions of tissue where tissue has been lost or damaged, such as abrasions, burns, and the like.

The matrix materials of the present invention will comprise a non-biologic polymer component, as described in more detail below. The non-biologic polymers will be selected to provide for bonding of the resulting layer of matrix material, typically providing a peel bond strength of at least about 0.03 N/cm, preferably at least about 0.07 N/cm, and usually in the range from about 0.07 N/cm to about 0.2 N/cm. Peel bond strength can be measured by conventional techniques. A particular method for measuring peel bond strength is as follows. Pieces of the matrix material (1.5 cm x 3 cm) are cut and glued to a plastic tab (1.5 cm x 3 cm) which overlaps the test material by 1 cm over the width (the 1.5 cm dimension), using a cyanoacrylate glue. A hole is pierced in the tab, and the test material bonded to the tissue *in vivo* or *in vitro*. A digital force gauge, such as an Omega DFO51-2 fitted with a 2 pound force transducer, Omega Instruments, Stamford, Connecticut, is attached to the plastic tab using a hook attachment which is secured to hole in the plastic tab. A manual upward force is then applied on the force gauge, and the sample peeled off with an even rate of pull, typically about 3 cm per second. Peel strengths are recorded in force (Newtons) divided by the width of the sample (1.5 cm) in order to determine the peel bond strength. The peel bond strength is measured as a maximum.

The non-biologic polymer component may comprise one, two, or more individual non-biologic polymers. Useful non-biologic polymers include acrylates, vinyl resins, polylactate-glycolides, polycaprolactones, polyoxyethylene, polyoxpropylene, and the like. Acrylates include thermoplastic and thermosetting resins which are polymers or copolymers of acrylic acid, methacrylic acid, esters of these acids, and acrylonitrile. Exemplary acrylates include polyacrylic acid, polyhydroxyethylmethacrylate, and polyacrylamide. Vinyl resins are polymers or copolymers of vinyl monomers. Exemplary vinyl resins include polyvinyl alcohol (PVA), polyvinylpyrrolidone and composites of polyoxyethylene, polyoxypropylene, and polylactate. Other useful synthetic polymers include polylactate-glycolide and

polycaprolactone. The non-biologic polymer may comprise substantially all of the matrix material, or may comprise only a portion thereof. In the latter case, additional components may be included, such as carrier substances, reinforcing materials (e.g., reinforcing meshes, fibers, filaments, braids and the like), and plasticizers. Exemplary carrier substances include collagen and gelatin.

The matrix material will usually be in the form of a solid layer, e.g., in the form of a sheet, film, patch, strip, mesh, or the like. The use of a mesh allows tissue to form a coagulum within the interstices of the mesh as energy is applied, as described in copending application serial no. 08/303,336, the disclosure of which is incorporated herein by reference. As mentioned above, the solid phase forms of the matrix material may optionally be reinforced with filaments, braids, meshes, and other woven and non-woven reinforcement materials. Usually, the reinforcement materials will be non-bioabsorbable so that they will remain even after the fusible material has been resorbed. Exemplary reinforcement materials include polymeric braids or meshes, particularly composed of polypropylene (Marlex®), fluorinated hydrocarbon polymers (Gore-Tex®), polyesters (such as Dacron®), and the like. In other cases, the reinforcement materials may be biodegradable. Exemplary biodegradable materials include polylactic acid, polyglycolic acid, copolymers of lactic acid and glycolic acid, polyhydroxybutyrate, other poly (α-hydroxy acids) polydioxanone, and the like in filaments, braids, meshes, woven and non-woven forms may be used.

Reinforced and non-reinforced matrix materials may be formed by conventional techniques for forming and solidifying synthetic polymers. Usually, the non-biologic polymer will be cross-linked to enhance structural integrity. For example, cross-linked copolymers may be formed by selecting at least one monomer to be polyethylenically unsaturated, with the second monomer being monoethylenically unsaturated. The degree of cross-linking can then be controlled by adjusting the ratio of monoethylenically unsaturated to polyethylenically unsaturated monomer. Usually

the polymers will be cast into sheets and the sheets will typically have a thickness in the range from about 0.005 mm to about 0.03 mm, usually from about 0.01 mm to about 0.2 mm. The sheets will preferably have an area of at least about 0.5 cm^2, preferably at least about 1 cm^2, and usually in the range from about 1 cm^2 to about 100 cm^2. It will be appreciated that sheets of various sizes can be trimmed to an appropriate size and shape for a particular application.

Alternatively, the matrix materials may be applied to the target region on the tissue in a non-solid dispersible state, e.g., as a liquid, gel, paste, spray, sol or combination thereof. Such dispersible matrix materials may be applied using syringes, brushes, sprayers, spatulas, or other methods suitable for spreading or dispersing a layer of the material over the wound region. Usually, the layer will have a thickness in the range from about 0.01 mm to 5 mm, preferably from about 0.05 mm to 1 mm.

The method of the present invention will utilize energy of a type and in an amount sufficient to fuse the matrix material including the non-biologic polymer to underlying tissue. Suitable energy sources include electrical energy, particularly radio frequency (RF) energy, heat energy, laser energy, ultrasonic energy, infrared, microwave, and the like. Preferred are the use of RF energy sources, such as those available as electrosurgical power supplies from companies such as Valleylab, Boulder, Colorado, and Con-Med, Utica, New York, employing conventional RF-applying probes. Particularly preferred are modified RF energy sources which provide for a dispersed or distributed current flow from a hand-held probe to the tissue. One such RF energy source is referred to as a radio frequency inert gas device or inert gas beam coagulator which relies on flow of an inert ionizable gas, such as argon, for conducting current from the probe to the tissue. Such inert gas beam coagulators are available commercially from suppliers such as Con-Med and Valleylab.

Energy from the energy source is typically directed to the tissue using a probe connected to an external power supply. The treating physician directs the probe manually to

apply energy over the surface of the matrix material and visually confirms that fusion has been achieved. Using an inert gas beam coagulator an energy output from about 2W to about 100W, preferably from about 20W to about 40W, will be used. The fusible material will typically be exposed to the energy for a total time from about 5 seconds to about 120 seconds, usually from about 5 seconds to about 20 seconds, for each 1 cm^2 of patch area. The precise timing will depend on the physician's visual assessment that the matrix material has fused to the underlying tissue.

Referring now to Fig. 1, an article 10 comprising a solid film or sheet 12 of matrix material comprising a non-biologic polymer component according to the present invention is illustrated. As shown, the sheet is square, but sheets having a variety of other regular and irregular geometries, such as rectangles, circles, ovals, and the like, could also be fabricated. The surface area, thickness, and other characteristics of the sheet 12 are preferably (but not necessarily) as described above.

The solid sheet 12 is usually packaged in a manner suitable to facilitate use by the treating physician. Generally, the sheet material is sterilized and packaged in a suitable container, such as a pouch, box, canister, bottle, or other conventional receptacle for medical products. In Fig. 2, the sheet 12 is illustrated as packaged in a pouch comprising a front sheet 14 and back sheet 16, where the sheets are laminated together around the edge to seal the interior of the package. Alternatively, the sheet material is rolled and packaged in order to provide larger areas of material. Sterilization of the sheet material 12 is accomplished, prior to, during, or after packaging. Suitable sterilization techniques include the use of sterilizing gases, sterilizing radiation, heat, or the like. Usually, the solid sheet 12 or other form of the material of the present invention will be packaged together with written instructions setting forth the methods described herein, i.e. that the materials are to be placed over a target site in tissue and energy applied to effect bonding. The instructions may be

printed on the packaging material (e.g. on a box or on a pouch holding the material) or may be provided on a separate package insert which is placed in or on the product package.

Referring now to Figs. 3 and 4, the use of a strip 20 of the matrix material of the present invention for covering and sealing a wound W in a region of tissue T is illustrated. The strip 20, which has been be trimmed to size prior to use, is placed over the wound W as shown in Fig. 4. After placement of the strip 20, energy such as radio frequency energy is applied over the strip using a hand-held probe 22, as illustrated in Fig. 4. The energy will be applied by passing the probe 22 over the upper, exposed surface of the strip to fuse the non-biologic polymer-containing strip to the underlying tissue. Exemplary power levels, exposure times, and the like, are described above.

Referring now to Figs. 5 and 6, an alternative method for applying matrix material to the wound W on the region of tissue T is illustrated. Liquid or gel matrix material 30 is applied using a syringe 32, typically in a series of parallel strips 34. Other patterns of application, of course, could also be employed, such as circular, spiral, criss-crossed, and the like. It is generally desirable, however, that material be applied at a relatively uniform density over the tissue, so that, after application of energy, a generally continuous layer of matrix material 36 results, as shown in Fig. 6. Again, the energy is typically applied using the hand-held probe 22.

Referring now to Fig. 7, after the application of energy, the matrix material is in the form of a generally continuous layer 40 of material which adheres to the upper surface S of the tissue T. The layer 40 of material will adhere to the tissue T with a minimum peel bond strength as set forth above. Moreover, the layer 40 will have a relatively high tensile strength so that it can maintain the integrity of the tissue T over the wound W.

The following examples re offered by way of illustration, not by way of limitation.

EXPERIMENTAL

Summary

Patches were fabricated from polyacrylamide. All patches were cross-linked to prevent dissolution in aqueous buffers. Patches of polyacrylamide were successfully welded to porcine lung in vitro with the argon beam coagulator. The patches which successfully welded were thinner (0.01 to 0.2mm thick) and were uniform sheets several cm^2 in area. Those that failed to weld were thick (>0.2 mm) or were curled, or small pieces (<1 cm^2 in area). We believe that the geometry of the patch is a very important factor in welding success.

Polyacrylamide patches

Acrylamide solution 0.62 ml in water (30% acrylamide, 0.8% N,N'-methylene-bis-acrylamide, w/v) was mixed with 1.86 ml 0.9% aq. sodium chloride, 22 ul of a 10% (w/v) solution of ammonium sulfate, and 5 ul of TEMED (tetramethylene-ethylenediamine) in polystyrene weighing boats 4.6 cm square. The solution polymerized within about 30 minutes at room temperature, and the resultant gel was allowed to dry overnight to a film. films of varying thickness could be prepared, depending on depth of the solution in the boat. Films between 0.3 and 1.0 mm thick were moistened and placed on an excised, inflated porcine lung and subjected to argon beam radiofrequency energy from the Birtcher 6400 ABC at 40 watts nominal power setting and an argon flow of 41/min. time of welds was 5-20 sec/cm^2 patch area. Thinner films bonded with peel strengths of approximately 0.05 to 0.2 N/cm. Thicker films failed to bond, apparently due to arcing of the beam around the patch, instead of through it.

Composite Polyacrylamide-Albumin patches

Albumin-polyacrylamide composite patches were prepared by mixing 167 mg bovine serum albumin, 1.67 ml saline, 0.62 ml stock acrylamide (30% aqueous acrylamide, 0.8% bis-acrylamide, w/v), 40 ul 10% (w/v) ammonium persulfate, and 8 ul TEMED (tetramethyl-ethylenediamine). The mixture was poured into several polystyrene weigh boats (4.6 cm square)

and allowed to polymerize at room temperature. Gels were allowed to dry at ambient to form moist mats and wrapped with plastic sheeting to prevent further drying. Moist mats were bonded by argon beam to porcine lung in vitro and yielded a peel strength of approximately 0.03 Newtons/cm; mats hydrated 5 min in saline did not bond after argon beam treatment. Mats were removable from the bond site in an intact state. Conditions for bonding with the argon beam were as for albumin patches as described above.

Although the foregoing invention has been described in some detail by way of illustration and example, for purposes of clarity of understanding, it will be obvious that certain changes and modifications may be practiced within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. A method for fusing a matrix material to tissue, said method comprising:

providing a matrix material containing a non-biologic polymer component which binds to tissue upon the application of energy;

placing the matrix material over a target location on the tissue; and

applying energy to the matrix material in an amount sufficient to fuse the matrix material to the tissue.

2. A method as in claim 1, wherein applying energy to the matrix material results in a layer of material which fuses to the underlying tissue with a peel bond strength of at least 0.03 N/cm.

3. A method as in claim 1, wherein the layer has a substantially continuous surface area of at least about 0.5 cm^2.

4. A method as in claim 1, wherein the layer has a thickness of at least about 0.01 mm.

5. A method as in claim 1, wherein the non-biologic polymer is selected from the group consisting of acrylates, polyvinyl resins, polylactate-glycolides, polycaprolactones, polyoxyethylenes, and polypropylethylenes.

6. A method as in claim 1, wherein the matrix material comprises the non-biologic polymer and a carrier substance.

7. A method as in claim 6, wherein the carrier substance is selected from the group consisting of collagen or gelatin.

8. A method as in claim 1, wherein the matrix material comprises a solid or mesh layer.

9. A method as in claim 1, wherein the matrix material comprises a dispersible, non-solid phase selected from the group consisting of liquids, gels, sols, suspensions, and powders.

10. A method as in claim 1, wherein the matrix material is placed over a wound at the target location in the tissue to help close the wound.

11. A method as in claim 1, wherein the energy is applied at a level in the range from 1 W/cm^2 to 100 W/cm^2 for a time sufficient to fuse the matrix material to the tissue without a substantial loss of mechanical strength.

12. A method as in claim 1 wherein the energy applying step comprises applying energy from the group consisting of radio frequency energy, heat energy, laser energy, microwave, infrared, and ultrasonic energy.

13. A method as in claim 12, wherein the energy is radio frequency energy.

14. A method as in claim 13, wherein the energy applying step comprises directing energy from a radio frequency inert gas coagulator applicator against the matrix material at the target location.

15. An improved method of the type wherein a matrix material is fused to tissue upon the application of energy, wherein the improvement comprises providing a matrix material including a non-biologic polymer component which binds to tissue upon the application of energy.

16. An improved method as in claim 15, wherein the non-biologic polymer is selected from the group consisting of

acrylates, polyvinyl resins, polylactate-glycolides, polycaprolactones, polyoxyethylenes, and polypropylethylenes.

17. An improved method as in claim 15, wherein the matrix material comprises the non-biologic polymer and a carrier substance.

18. An improved method as in claim 17, wherein the carrier substance is selected from the group consisting of collagen and gelatin.

19. An improved method as in claim 15, wherein the matrix material comprises a solid or mesh layer.

20. An improved method as in claim 15, wherein the matrix material comprises a dispersible, non-solid phase selected from the group consisting of liquids, gels, sols, suspensions, and powders.

21. A tissue closure matrix material comprising a non-biologic polymer component which binds to tissue upon the application of energy.

22. The material as in claim 21, which binds to the underlying tissue with a peel bond strength of at least about 0.03 N/cm.

23. The material as in claim 21, wherein the sheet has a substantially continuous surface area of at least about 0.5 cm^2.

24. The material as in claim 21, wherein the sheet has a thickness of at least about 0.01 mm.

25. The material as in claim 21, wherein the non-biologic polymer is selected from the group consisting of acrylates, polyvinyl resins, polylactate-glycolides, polycaprolactones, polyoxyethylenes, and polypropylethylenes.

26. The material as in claim 21, wherein the matrix material comprises the non-biologic polymer and a carrier substance.

27. The material as in claim 26, wherein the carrier substance is selected from the group consisting of collagen and gelatin.

28. A package containing the material of claim 21, wherein the package is sealed and the article is sterilized therein.

29. The package of claim 28, further comprising written instructions to place the material over tissue and to apply energy to the material and tissue to bond the material to the tissue.

30. The material as in claim 21, wherein the matrix material comprise a solid or mesh layer.

31. The material as in claim 21, wherein the matrix material comprises a dispersible, non-solid phase selected from the group consisting of liquids, gels, sols, suspensions, and powders.

32. The material as in claim 21, wherein the polysaccharide component binds with the application of energy at a level in the range from about 1 W/cm^2 to about 100 W/cm^2 for a time selected to fuse the matrix material to the tissue.

33. The material as in claim 31, wherein the energy is from a radio frequency inert gas device.

34. An article comprising:

a film of a tissue closure material comprising a polyacrylate component,

a sealed package holding the film, wherein the film is sterilized therein; and

written instructions to place the film over tissue and to apply energy to the film and the tissue to bond the material to the tissue.

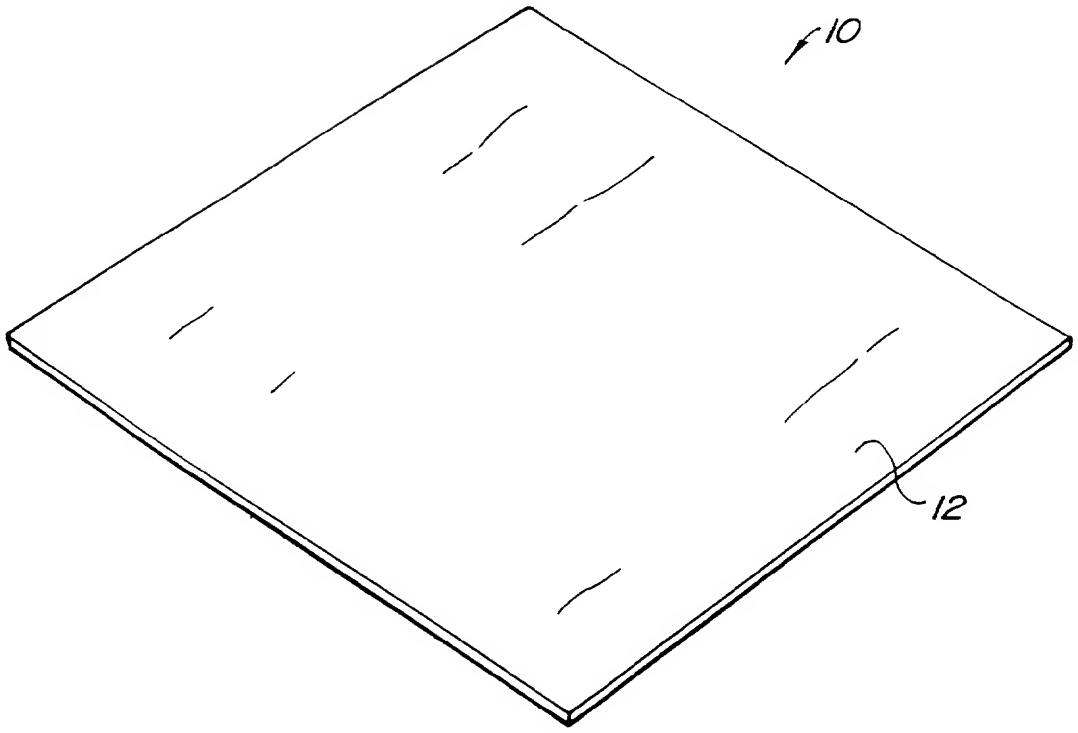

FIG. 1.

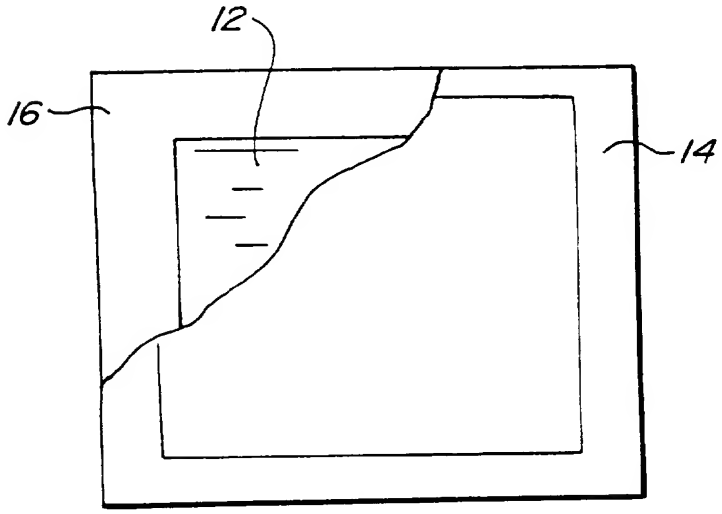

FIG. 2.

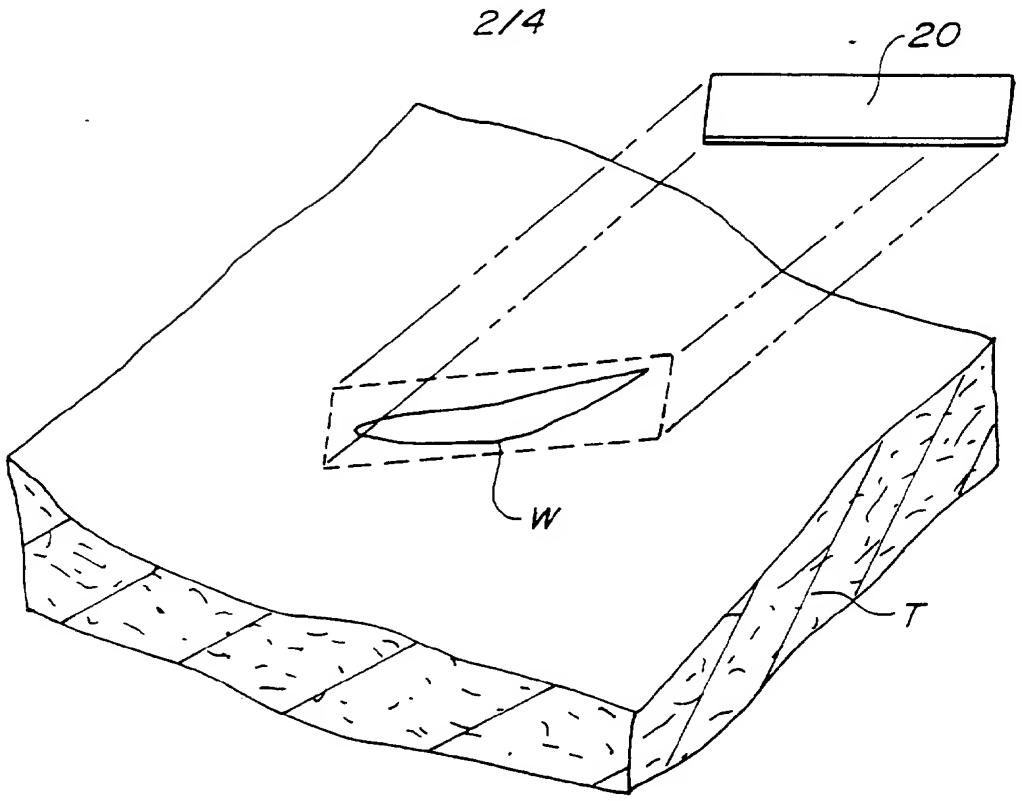

FIG. 3.

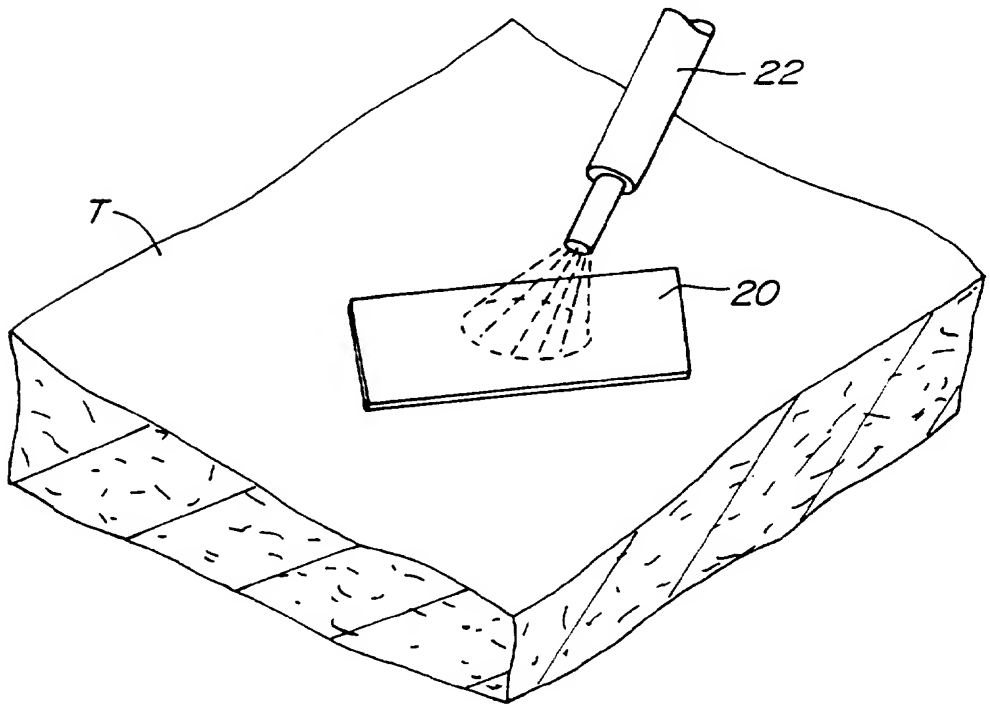

FIG. 4.

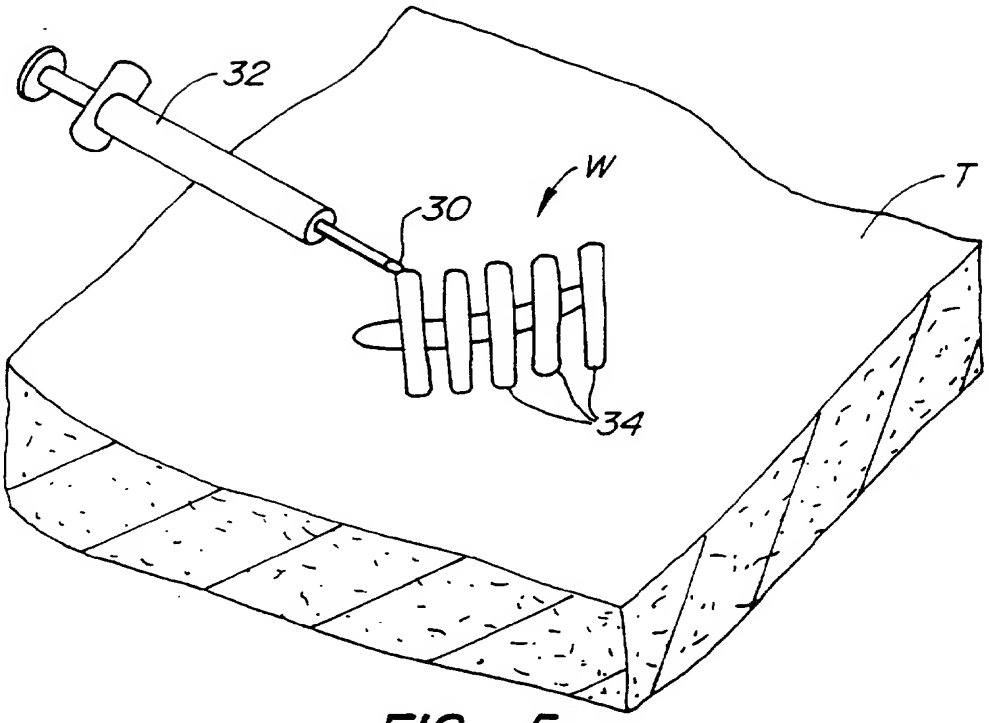

FIG. 5.

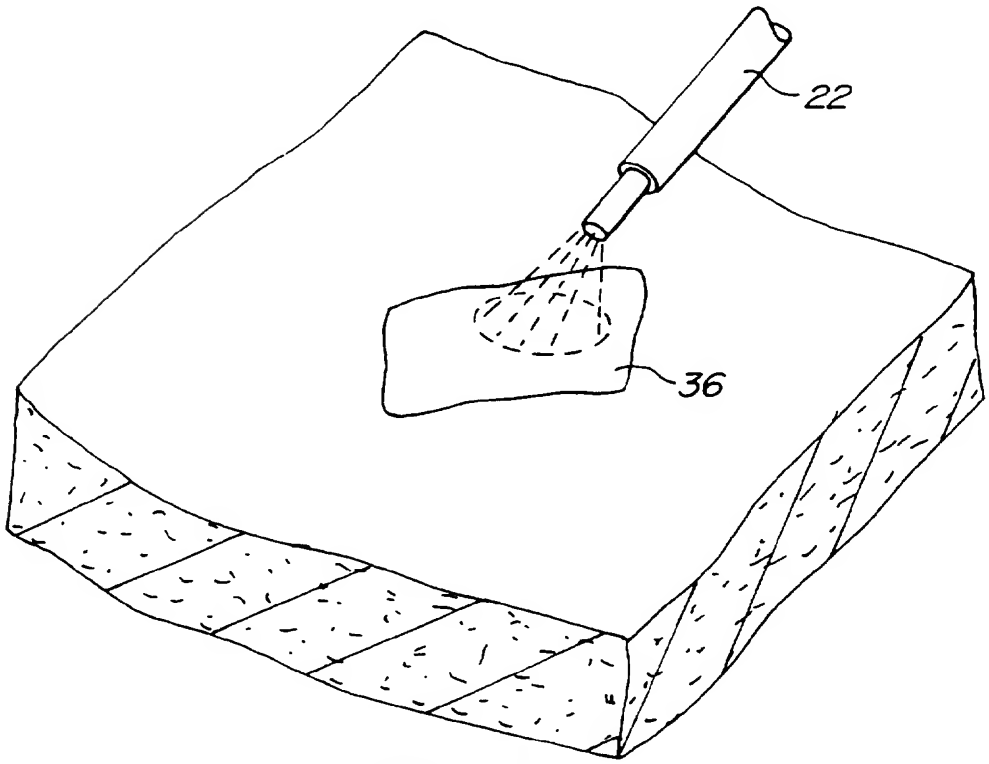

FIG. 6.

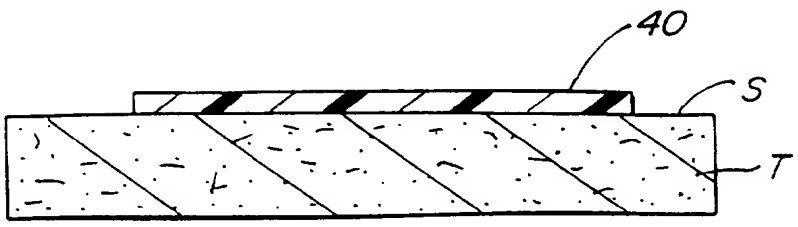

FIG. 7.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/17846

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 17/08
US CL :606/213, 214

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/213, 214

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,226,877 A (EPSTEIN) 13 July 1993, col. 1, lines 12-16; col. 4, lines 1-12; and col. 6, lines 20-23	1, 4-6, 9, 10, 15-17, 20, 21, 24-26, 31 --- 28
X	US 5,464,471 A (WHALEN et al) 07 November 1995, col. 1, lines 49-54.	1, 5, 8, 10, 15, 16, 19, 21, 25, 30
Y	US 3,527,224 A (RABINOWITZ) 08 September 1970, col. 2, lines 56-61.	28

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
04 JANUARY 1997	31 JAN 1997
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3590	Authorized officer TINA T. D. PHAM Telephone No. (703) 308-0824

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